UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,374	01/29/2004	Avi Ashkenazi	P1216R1C1D1	4761

9157 7590 01/13/2005

GENENTECH, INC.
1 DNA WAY
SOUTH SAN FRANCISCO, CA 94080

EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/767,374	Applicant(s) ASHKENAZI ET AL.	
	Examiner Maher M. Haddad	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *49-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *49-54, 56 and 58-59* is/are rejected.

7)☒ Claim(s) *55 and 57* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/19/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 49-59 are pending and under consideration.

2. The specification on page 1 should be amended to reflect the status of parent application No. 09/953,499 and 09/254,465.

3. The amendment filed 01/29/04 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows:

The amendment for "incorporated by reference" to U.S. application 09/254,465, PCT/US98/24855, provisional Application 60/078,936 and PCT/US98/19437 on page 1, line 7 of the specification does not enjoy the status as part of the original disclosure in the application.

4. The U.S. Patents 6,838,554 and 6,410,708 cited on the PTO FORM 892 is issued from the parental application serial No. 09/953,499 and 09/254,465.

5. Applicant's IDS, filed 4/19/04, is acknowledged, however, the BLAST results provided as reference number 15-17 are not appropriate for an IDS. BLAST alignments should be appended as part of each individual sequence reference, which must include at a minimum the Accession No., Database and earliest available date of the reference sequence in order to be appropriate for inclusion in the IDS.

6. Applicant's amendment to the specification on page 68, line 34, filed 01/29/04, which assures that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent, satisfies the requirement for the deposit of the biological material of cDNA deposited under ATCC accession number 209620 under 35 USC § 112, first paragraph.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 49-54, 56 and 58-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide molecule having the amino acid sequence of the polypeptide of SEQ ID NO:2 to stimulates the proliferation of T-lymphocytes, does not reasonably provide **enablement** for an isolated polypeptide molecule having "at least

80%, 85%, 90%, 95%, or 99%" amino acid sequence identity to the amino acid sequence of the polypeptide of SEQ ID NO:2, the amino acid sequence of the polypeptide of SEQ ID NO:2, lacking its associated signal peptide, or the amino acid sequence of the polypeptide encoded by the full-length coding sequence of the cDNA deposit under ATCC accession number 209620, wherein said polypeptide molecule stimulates the proliferation of T-lymphocytes in claims 49-53, respectively, or an isolated polypeptide molecule comprising the amino acid sequence of the polypeptide of SEQ ID NO: 2, lacking its associated signal peptide in claims 54 and 56 or a chimeric polypeptide comprising a polypeptide molecule of claim 54 fused to a "heterologous polypeptide" in claim 58. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification does not provide a sufficient enabling description of the claimed invention. The specification discloses only a single amino acid sequence (SEQ ID NO:2, PRO362) encoded SEQ ID NO:7 with a disclosed activity of stimulating the proliferation of T-lymphocytes (e.g., examples 5-6). The instant claims encompass in their breadth *any* amino acid "with at least about 80, 85, 90, 95 or 99% identity to SEQ ID NO:2; or a chimeric polypeptide fused to any heterologous polypeptide.

However, there does not appear to be sufficient guidance in the specification as filed as to how the skilled artisan would make and use the various amino acids recited in the instant claims. A person of skill in the art would not know which sequences are essential, which sequences are non-essential, and what particular sequence lengths identify essential sequences. There is insufficient guidance to direct a person of skill in the art to select particular sequences or sequence lengths as essential for to stimulate the proliferation of T-lymphocytes. Without detailed direction as to which amino acid sequences are essential to the function of the claimed polypeptide, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of amino acid sequences encompassed by the instant claims would share the ability to stimulate the proliferation of T-lymphocytes of the claimed polypeptide of SEQ ID NO:2, other than the amino acid of SEQ ID NO:2 encoding SEQ ID NO:7.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. Thus, it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. The similarity or dissimilarity between two protein's amino acid sequence does not provide conclusive evidence of structural and therefor functional similarity. It is well known the amino acid sequence of a protein dictates its folding into a specific three-dimensional conformation, the native state and that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression and protein. Therefore, structurally unrelated polypeptide having "at least 80, 85, 90, 95, or 99%" identity to the amino acid sequence of SEQ ID NO:2 would be expected to have greater differences in their activities. Since the amino acid sequence of a protein determines its structure and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality requires knowledge of, and guidance with regard to which amino acid in the protein's sequence, if any, are tolerant of modification and which are conserved and detailed knowledge of the ways in which a polypeptide's structure relates to it's functional usefulness. However, the problem of predicting protein structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain binding or functional aspects of PRO362, and finally, what changes can be tolerated with respect thereto is complex and well outside the realm of routing experimentation.

The terms "having" recited in claims 49-53 and "comprising" recited in claims 54, 56 and 58 are open ended and extend the claimed polypeptide molecule to include additional non-recited amino acids on either or both C-terminal or N-terminal of SEQ ID NO: 2 or the SEQ ID NO:2, lacking its associated signal peptide.

Claims 49-54 and 56 recite a polypeptide molecule that is "lacking its associated signal peptide". However, the specification does not provide guidance on what signal peptide can be removed. Further the specification is silence with regard to the length and position of the signal peptide. The specification provides insufficient direction for the skilled artisan to predict the location of signal peptide cleavage sites in amino acid sequence of SEQ ID NO:2.

Claim 58 recites "a heterologous polypeptide". However, besides an epitope tag and an Fc region of an immunoglobulin, the specification fails to disclose what other heterologous polypeptide can be fused to the claimed polypeptide of SEQ ID NO:2 and at the same time would maintain the structure and function as polypeptide of SEQ ID NO:2.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. Claims 54, 56 and 58-59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of an isolated polypeptide molecule having the amino acid sequence of the polypeptide of SEQ ID NO:2 to stimulates the proliferation of T-lymphocytes.

Applicant is not in possession of an isolated polypeptide molecule comprising the amino acid sequence of the polypeptide of SEQ ID NO: 2, lacking its associated signal peptide in claims 54 and 56 or a chimeric polypeptide comprising a polypeptide molecule of claim 54 fused to a "heterologous polypeptide" in claim 58.

Applicant has disclosed only amino acid of SEQ ID NO: 2; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims, with regard to the "lacking its associated signal peptide" or the "heterologous polypeptide". Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

10. No claim is allowed.

11. Claim 55 and 57 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
January 7, 2005

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600